

### Remarks

Prior to entry of this amendment, claims 19-24, 26, 30-34, 36, 38, 41-46 and 49 are pending. By this filing, claim 19 is amended to incorporate suggestions made by the Examiner during the telephone interview discussed more fully below. No other amendments are made; thus, once this paper is entered, **claims 19-24, 26, 30-34, 36, 38, 41-46 and 49 will still be pending**, and believed to be in condition for allowance.

Entry of this amendment is proper because it enters suggestions made by the Examiner, and would make any remaining issues more clear upon Appeal if such becomes necessary.

#### *Examiner Interview*

Applicants thank the Examiner for taking time to interview this case with their undersigned representative on September 15, 2008. The rejections of claim 19 under §112, first paragraph, were discussed during the interview. It is believed that agreement was reached regarding how to overcome all of the pending rejections, and this document has been prepared in view of that agreement and keeping in mind suggestions made by the Examiner.

#### *Rejections of Claim 19 under 35 U.S. C. §112*

Claim 19 (and all claims that depend therefrom) are rejected under §112, first paragraph, as allegedly failing to comply with the enablement requirement. It appears that this rejection has two components: relating to step b) of claim 19; and to step c)(i) and step (i) of claim 19. Applicants traverse these rejections and will address each separately below.

First, it is alleged that “Claim 19 is not enabled because there does not appear to be a coenzyme/cosubstrate provided in step b) of the claim.” Applicants traverse this rejection, at least because the claim contains reference to everything essential to carry out the claimed method, particularly when it is read in the context of the specification. As discussed during the interview, claim 19 explicitly requires that the method take place in the presence of “a reaction mixture comprising a non-limiting amount of one or more substrates necessary for activity of the PDH complex”. Anyone of ordinary skill would understand what is required for a PDH reaction *in vitro*. In addition, the claim

language is given context in the specification, for instance at least at page 2 [0005], Figure 1 and the accompanying legend (at page 6 [0018]), the methods and discussion of the examples (*e.g.*, page 25 [0078]; page 26 [0080]), and so forth. Given the level of skill in the art, the long familiarity in the art with methods of carrying out PDH reactions *in vitro*, and Applicants specific teachings, claim 19 step b) is enabled without any amendment.

Further, it is alleged that claim 19 is “circular in that step c)(i) calls for the measurement of NADH production while step i) of the claim calls for the transfer of an electron from NADH to NAD<sup>+</sup> for the detection. It is not seen how the artisan could measure the same activity by measuring both the production of NADH and NAD<sup>+</sup> in opposition to one another.” Applicants traverse this rejection, as it arises from a misreading of claim 19.

As discussed with the Examiner during the interview, claim 19 encompasses multiple ways of measuring activity of PDH complex, two categories of which are separated by the word “or” between subparts (i) and (ii) of claim 19 part c). Subpart c)(i) encompasses measurement of the activity of PDH– that is, detecting “the amount of NADH produced in the reaction mixture” – which can be carried out either directly or indirectly (as now detailed in parts (1) and (2) of claim 19). In contrast, subpart c)(ii) encompasses measuring the amount of PDH phosphorylation as an indirect measurement of relative activity. Applicants believe the amendments made to claim 19 (which reflect rearrangement of the existing text and corrections to clarify antecedent basis) help to make this clear, and to clarify that PDH activity can be measured either by measuring NADH or NAD<sup>+</sup> levels in a reaction – just not the same reaction.

In view of the above discussion, and the amendment submitted herewith, Applicants request withdrawal of the enablement rejection of claim 19. It is believed that this claim is allowable as written.

**Conclusion**

Based on the foregoing amendment and comments, the pending claims are in condition for allowance and notification to this effect is requested. If any questions remain before the claims can be allowed, the Examiner is invited to telephone the undersigned.

Respectfully submitted,

KLARQUIST SPARKMAN, LLP

One World Trade Center, Suite 1600  
121 S.W. Salmon Street  
Portland, Oregon 97204  
Telephone: (503) 595-5300  
Facsimile: (503) 595-5301

By /Tanya M. Harding/  
Tanya M. Harding, Ph.D.  
Registration No. 42,630